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10/582,413	10/26/2006	Toshihiko Ohtomo	14875-164US1 CI-A0321P-US	7418
26161	7590	04/16/2010	EXAMINER	
FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			DUFFY, BRADLEY	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

<b>Office Action Summary</b>	Application No. 10/582,413	Applicant(s) OHTOMO ET AL.	
	Examiner BRADLEY DUFFY	Art Unit 1643	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period **will** apply and **will** expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply **will**, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 October 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 40-42, 49, 50, 54, 55, 58 and 59 is/are pending in the application.
- 4a) Of the above claim(s) 55 and 58 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 40-42, 49, 50, 54 and 59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/24/09, 12/11/09, 1/15/10</u>                               | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 11, 2009, has been entered.

2. The amendment filed December 11, 2009, is acknowledged and has been entered. Claims 43-48, 51-53, 56 and 57 have been canceled. Claims 40, 41, 54, 55 and 59 have been amended.

3. Claims 40-42, 49, 50, 54, 55, 58 and 59 are pending. Claims 55 and 58 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

4. Claims 40-42, 49, 50, 54 and 59 are under examination.

### ***Election/Restrictions***

5. Starting at page 6 of the response filed December 11, 2009, Applicant has requested further consideration of the withdrawal of claims 55 and 58 as being drawn to a nonelected invention. In the response Applicant argues that in an interview with the prior Examiner, Examiner Gussow, essentially the same subject matter was presented and Examiner Gussow indicated that such subject matter was part of the elected invention and further argues that MPEP 704.01 indicates that when an application has received an action by some other examiner that full faith and credit should be given to the search and action of the previous examiner. Accordingly, based on these considerations, Applicant

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requests that claims 55 and 58 be examined with the elected invention.

In response as set forth in 37 CFR 1.2:

All business with the Patent and Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

Notably, in this case, the prior Examiner did not enter or otherwise examine claims drawn to the subject matter of claims 55 and 58 and it is not apparent how (or if) the subject matter presented in the interview is essentially the same as the subject matter withdrawn from consideration. Notably, the record does not state that Examiner Gussow considered methods that require identification of *two* different antibodies which bind different epitopes to be part of the elected invention which is limited to methods that recite identifying one antibody to improve its activity.

As set forth in the action mailed March 11, 2009, the methods of claims 55 and 58 do not relate to the same single general inventive concept under PCT Rule 13.1 as the method of claim 41 which is part of the originally elected invention 41, because, under PCT Rule 13.2, they lack the same or corresponding special technical feature.

In this case, it is apparent that claims 55 and 58 are drawn to methods that have a different special technical feature than the special technical feature of the elected invention because claims 55-58 do not recite the method objective of the elected invention and require two antibodies, while the elected invention enhances the activity of a singular antibody. Accordingly, the methods steps of the elected invention are not required in the methods of claims 55 and 58 and the method steps of claims 55 and 58 are not required in the methods of the elected invention. Therefore, it is maintained that the methods of claims 55 and 58 do not relate to the same single general inventive concept under PCT Rule 13.1 as the elected invention. Furthermore, it is noted that PCT Rules 13.1 and 13.2 do not provide for a single general inventive concept to comprise more than the first

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mentioned product, the first mentioned method for making said product, and the first mentioned method for using said product. Accordingly, the methods set forth in claims 55 and 58 do not form a single general inventive concept with the original elected method.

Finally, Applicant has not otherwise provided any arguments or scientific reasoning which would establish that claims 55 and 58 are drawn to methods that have a same special technical feature as the special technical feature of the elected invention.

For these reasons and the reasons of record, and after careful and full consideration of Applicant's response, it is maintained that the subject matter of claims 55 and 58 are drawn to methods that have a different special technical feature than the special technical feature of the elected invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 55 and 58 are withdrawn from consideration as being directed to a nonelected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

#### ***Information Disclosure Statements***

6. The references cited in the information disclosure statements filed on 11/24/09, 12/11/09 and 1/15/10 have been considered. Furthermore, while considered, the Office Actions, Office Action responses, Search reports and other foreign patent office actions cited on these information disclosure statements have been crossed out because these citations clearly do not conform to the information disclosure statement requirements and are not suitable for printing on the issued patent. See MPEP 609.

#### ***Grounds of Rejection Withdrawn***

7. Applicant's amendment and/or arguments filed December 11, 2009, have obviated or rendered moot the grounds of rejection set forth in the previous

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Office action mailed June 25, 2009.

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 103***

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 40-42, 49, 50, 54 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over by WO 2002/033072 A1 (Tsuchiya et al, 2002, IDS filed 5/23/07) as evidenced by US PG PUB 2004/0091475 A1 (Tsuchiya et al, 2004,

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IDS filed 5/23/07). Since WO 2002/033072 A1 is written in Japanese, the page numbers of US 2004/0091475 A1, which is the publication of the national stage entry application of WO 2002/033072 A1, will be cited to evidence the teachings of this publication.

The claims are herein drawn to methods comprising:

- (a) identifying an antibody that binds to mpl receptor;
- (b) providing the antibody's light chain variable region amino acid sequence and heavy chain variable region amino acid sequence; and
- (c) producing an sc(Fv)<sub>2</sub> or covalently linked scFv multimer comprising two or more copies of said light chain variable region sequence of (b) and two or more copies of said heavy chain variable region sequence of (b), linked via linkers,
- (d) testing the sc(Fv)<sub>2</sub> or covalently linked scFv multimer for said TPO-like agonistic activity (TPO)-like agonistic activity, wherein the TPO-like agonistic activity is stimulating cell proliferation by activating myeloproliferative leukemia virus oncogene (mpl) receptor; and
- (e) selecting the sc(Fv)<sub>2</sub> or covalently linked scFv multimer if it binds to mpl receptor and exhibits said TPO-like agonistic activity at a level that is (i) greater than the level at which the antibody of (a) exhibits the same activity and (ii) greater than the level at which a diabody exhibits the same activity, the diabody consisting of two identical, non-covalently associated single-chain polypeptides, each of which consists of one copy of said light chain variable region sequence of (b) linked via a linker to one copy of said heavy chain variable region sequence of (b). The claims are further drawn to the antibody being human or humanized, or wherein the sequence of the sc(Fv)<sub>2</sub> comprises, in order: the heavy chain variable region sequence, a first linker sequence, the light chain variable region sequence, a second linker sequence, the heavy chain variable region sequence, a third linker sequence, and the light chain variable region sequence.

WO 2002/033072 A1 teaches methods comprising

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- (a) identifying an antibody that binds to mpl receptor;
- (b) providing the antibody's light chain variable region amino acid sequence and heavy chain variable region amino acid sequence;
- (c) producing an sc(Fv)<sub>2</sub> or covalently linked scFv multimer comprising two or more copies of said light chain variable region sequence of (b) and two or more copies of said heavy chain variable region sequence of (b), linked via linkers; and
- (d) testing the sc(Fv)<sub>2</sub> or covalently linked scFv multimer for said TPO-like agonistic activity (TPO)-like agonistic activity, wherein the TPO-like agonistic activity is stimulating cell proliferation by activating myeloproliferative leukemia virus oncogene (mpl) receptor (see entire document, e.g., pages 1-5 and 22 of US PG PUB 2004/0091475 A1). WO 2002/033072 A1 further teaches the antibody being human or humanized, or wherein the sequence of the sc(Fv)<sub>2</sub> comprises, in order: the heavy chain variable region sequence, a first linker sequence, the light chain variable region sequence, a second linker sequence, the heavy chain variable region sequence, a third linker sequence, and the light chain variable region sequence (see entire document, e.g., pages 3 and 4 and Figure 34 of US PG PUB 2004/0091475 A1).

Finally, while WO 2002/033072 A1 expressly teaches e.g., selecting modified antibodies "having TPO agonist action (ED50) more than two times higher than that of parent antibody, further preferably more than 5 times, most preferably more than 10 times" (see page 2, paragraph [0019] of US PG PUB 2004/0091475 A1) WO 2002/033072 does not expressly teach (e) selecting the sc(Fv)<sub>2</sub> or covalently linked scFv multimer if it binds to mpl receptor and exhibits said TPO-like agonistic activity at a level that is (i) greater than the level at which the antibody of (a) exhibits the same activity and (ii) greater than the level at which a diabody exhibits the same activity, the diabody consisting of two identical, non-covalently associated single-chain polypeptides, each of which consists of one copy of said light chain variable region sequence of (b) linked via a linker to one copy of said heavy chain variable region sequence of (b).



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However, this deficiency would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made based on the disclosed motivation of preferably selecting a modified antibody with higher TPO agonist activity. Notably, WO 2002/033072 A1 teaches one of skill in the art to make both covalent and non-covalent modified antibodies of a parent antibody having TPO agonist action (see e.g., pages 1 and 2 of US PG PUB 2004/0091475 A1), so one of skill in the art would have made both covalent and non-covalent modified antibodies having TPO agonist action, tested their activities and compared them to each other and the parent antibody and then would have been motivated to select the sc(Fv)<sub>2</sub> or covalently linked scFv multimer that binds to mpl receptor and exhibits said TPO-like agonistic activity at a level that is (i) greater than the level at which the antibody of (a) exhibits the same activity and (ii) greater than the level at which a diabody exhibits the same activity, the diabody consisting of two identical, non-covalently associated single-chain polypeptides, each of which consists of one copy of said light chain variable region sequence of (b) linked via a linker to one copy of said heavy chain variable region sequence of (b). Once again, one of skill in the art would have been motivated to practice such a selecting step since WO 2002/033072 A1 clearly teaches a preference for antibodies and having higher TPO agonist action as compared to another antibody having TPO agonist action. Finally, since WO 2002/033072 A1 clearly teaches testing and screening steps that monitor modified antibodies for TPO-like agonistic stimulation of cell proliferation one of skill in the art also would have had a reasonable expectation of success in practicing methods encompassed by the claims.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference.

### **Conclusion**

11. No claims are allowed.

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12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brad Duffy whose telephone number is (571) 272-9935. The examiner can normally be reached on Monday through Friday 7:00 AM to 4:30 PM, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully,  
Brad Duffy  
571-272-9935

/Stephen L. Rawlings/  
Primary Examiner, Art Unit 1643

/bd/  
Examiner, Art Unit 1643  
April 5, 2010